



US009636342B2

(12) **United States Patent**
Chen et al.

(10) **Patent No.:** **US 9,636,342 B2**

(45) **Date of Patent:** **May 2, 2017**

(54) **METHOD FOR TREATING PROSTATE
CANCER**

(71) Applicant: **UNIVERSITY OF SOUTH
CAROLINA**, Columbia, SC (US)

(72) Inventors: **Mengqian Chen**, Columbia, SC (US);
Igor Roninson, Lexington, SC (US)

(73) Assignee: **University of South Carolina**,
Columbia, SC (US)

(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/439,127**

(22) PCT Filed: **Nov. 1, 2013**

(86) PCT No.: **PCT/US2013/067990**

§ 371 (c)(1),

(2) Date: **Apr. 28, 2015**

(87) PCT Pub. No.: **WO2014/071143**

PCT Pub. Date: **May 8, 2014**

(65) **Prior Publication Data**

US 2015/0272953 A1 Oct. 1, 2015

Related U.S. Application Data

(60) Provisional application No. 61/721,134, filed on Nov.
1, 2012.

(51) **Int. Cl.**

A61K 31/517 (2006.01)

A61K 31/5377 (2006.01)

(52) **U.S. Cl.**

CPC **A61K 31/517** (2013.01); **A61K 31/5377**
(2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2006/0235034 A1* 10/2006 Neamati C07C 243/32
514/267

OTHER PUBLICATIONS

Haas, Michel J. CDK8 inhibitor: Senex's best thing. SciBX: Sci-
ence-Business eXchange. 5(33), Aug. 23, 2012, p. 1-3.*
Schmidt, Lucy J. Gene Expression in Prostate Cancer Cells Treated
With the Dual 5-Alpha-Reductase Inhibitor Dutasteride. Journal of
Andrology. 25(6), (2004), 944-953.*

* cited by examiner

Primary Examiner — Samantha Shterengarts

(74) *Attorney, Agent, or Firm* — Wayne A. Keown;
Verrill Dana LLP

(57) **ABSTRACT**

The invention provides a method for treating prostate cancer
in a subject comprising administering to the subject an
effective amount of a selective inhibitor of one or more of
CDK8 and CDK19. In some embodiments the inhibitor
inhibits CDK19. In some embodiments, the inhibitor inhib-
its CDK8 at a Kd of lower than 200 nM and/or inhibits
CDK19 at a Kd of lower than 100 nM. In some embodi-
ments, the prostate cancer is androgen independent. In some
embodiments, the prostate cancer is androgen independent
due to one or more of androgen receptor gene amplification,
androgen receptor gene mutation, ligand-independent trans-
activation of androgen receptor and activation of intracel-
lular androgen synthesis. In some embodiments, the inhibi-
tor inhibits increased activity of NF-κB. In some
embodiments, the inhibitor does not inhibit increased basal
levels of NF-κB. In some embodiments, inhibition of one or
more genes by AR is not inhibited.

6 Claims, 16 Drawing Sheets